Claims

1. The use of a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these, in the preparation of a medicament for use in the treatment of animals, in particular humans, for proliferative disease, and/or to inhibit angiogenesis.

2. The use of a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these, in the preparation of a medicament for use in the treatment of mucosal cancers.

3. The use according to claim 2 wherein the mucosal cancer is bladder cancer.

4. The use of a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these, in the preparation of a medicament for infusion into tumours.

5. The use according to claim 4 wherein the tumour is a solid tumour of an internal organ.

6. The use according to claim 5 wherein the internal organ is selected from brain, liver, kidney, prostate and ovaries.

7. The use according to claim 6 wherein the internal organ is brain.

8. The use according to claim 7 wherein the brain tumour is human glioblastoma.

9. The use of a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these, in the preparation of a medicament for use in the inhibition of angiogenesis.

10. The use according to claim 9 which is for slowing metastasis of tumour cells.

11. The use according to any one of the preceding claims wherein the biologically active complex comprises alpha-lactalbumin or a variant of alpha-lactalbumin which is in the apo folding state, or a fragment of either of any of these, and a cofactor which stabilises the complex in a biologically active form, provided that any fragment of alpha-lactalbumin or a variant thereof comprises a region corresponding to the region of α-lactalbumin which forms the interface between the alpha and beta domains.

12. The use according to claim 11 wherein the cofactor is a cis C18:1:9 or C18:1:11 fatty acid or a different fatty acid with a similar configuration.

13. The use according to any one of claims 1 to 10 wherein the biologically active complex comprises HAMLET, which is obtainable either by isolation from casein fractions of milk which have been precipitated at pH 4.6, by a combination of anion exchange and gel chromatography, or by subjecting α-lactalbumin to ion exchange chromatography in the presence of a cofactor from human milk casein, characterized as C18:1 fatty acid.

14. The use according to any one of claims 1 to 10 wherein the biologically active complex of α-lactalbumin comprises (i) a cis C18:1:9 or C18:1:11 fatty acid or a different fatty acid with a similar configuration; and

(ii) α-lactalbumin from which calcium ions have been removed, or a variant of α-lactalbumin from which calcium ions have been removed or which does not have a functional calcium binding site; or a fragment of either of any of these, provided that any fragment comprises a region corresponding to the region of α-lactalbumin which forms the interface between the alpha and beta domains.

15. The use according to claim 14 wherein the biologically active complex includes a variant of α-lactalbumin in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional.

16. The use according to claim 15 wherein the variant has a mutation at one of the amino acids equivalent to K79, D82, D84, D87 and D88 of bovine α-lactalbumin.

17. The use according to claim 16 wherein the modification is at D87 which includes a variant of α-lactalbumin having a D87A or D87N variants.

18. The use according to any one of claims 1 to 10 wherein the biologically active complex comprises a fragment of α-lactalbumin or a variant thereof, and where the fragment includes the entire region from amino acid 34-86 of the native protein.

19. The use according to any one of the preceding claims wherein the α-lactalbumin is human or bovine α-lactalbumin or a variant of either of these.

20. The use according to claim 19 wherein the α-lactalbumin is human α-lactalbumin.

21. The use according to claim 19 wherein the α-lactalbumin is mutant bovine α-lactalbumin which includes an S70R mutation.

22. A method for treating humans for proliferative disease, and/or to inhibit angiogenesis which comprises administering to said a patient, a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these.

23. A method for treating a mucosal tumour which comprises administering to said tumour in a patient in need thereof, a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these.

24. A method according to claim 23 wherein the mucosal tumour is bladder cancer.

25. A method according to claim 24 wherein the biologically active complex is administered by intra-vesical instillation.

26. A method according to claim 25 wherein from 200mg to 1g of the biologically active complex is administered in a single dosage unit.

27. A method according to claim 26 wherein the dosage unit is repeated on at least 5 days.

28. A method according to claim 27 wherein the dosage is given on consecutive days.

29. A method for treating cancer which comprises infusing into a tumour, a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these.

30. A method according to claim 29 wherein the complex is administered in the form of a composition further comprising a saline carrier.

31. A method according to claim 29 or claim 30 wherein the complex is infused using convection enhanced delivery (CED).

32. A method according to any one of claims 29 to 31 wherein the tumour is a tumour of the brain, liver, kidney, prostate and ovaries.

33. A method according to claim 32 wherein the tumour is a brain tumour.

34. A method according to claim 33 wherein the tumour is human glioblastoma.

35. A method for inhibiting angiogenesis which comprises administering to a patient in need thereof, a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these.

36. The use of a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these, in the preparation of a medicament for use in the treatment of malignant skin tumours, in particular melanoma.

37. A method for treating malignant melanoma, which method comprises applying a biologically active complex of α-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these, to the melanoma.

38. A method of treating cancer in particular in humans, *in-vivo*, by applying to the tumour, a biologically active complex comprising HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these.

39. The use of a biologically active complex comprising HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these in the preparation of a medicament for use in *in-vivo* human cancer therapy.